Voltammetric and in situ infrared spectroscopy studies of hydroxyurea electrooxidation at Au(111) electrodes in $HClO_4$ solutions.

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Abstract

The oxidation of hydroxyurea ($H_2NCONHOH$, HU) at Au(111) single crystal and Au(111)-25 nm thin film electrodes is studied spectroelectrochemically in $HClO_4$ solutions using external reflection infrared and Surface Enhanced Infrared Reflection Absorption Spectroscopy under Attenuated Total Reflection conditions (ATR-SEIRAS). The in situ external reflection spectra prove the formation of dissolved carbon dioxide and adsorbed cyanate during the electrooxidation of HU. The enhanced surface sensitivity of the ATR-SEIRAS experiments facilitates the detection of adsorbed cyanate and allows the observation of other adsorbate bands tentatively ascribed to reaction intermediates involving partial oxidation of the HU molecules, some of them corresponding to nitrosyl groups.

Keywords: Au(111); gold thin film ; hydroxyurea electrooxidation; external reflection infrared; ATR-SEIRAS

1. Introduction.

Hydroxyurea (HU, also named hydroxycarbamide, $NH_2CONHOH$) is a simple urea derivative used as an effective treatment against several cancers [1-4]. Some beneficial effects of HU seem to be related to the formation of nitric oxide [1,2]. Several papers have been published regarding HU oxidation by hydrogen peroxide [5,6], Fe(III) [7], hexacyanoferrate [8] and vanadium (V) [9]. In all cases, HU oxidation seems to proceed via the formation of a nitroxyl radical ($NH_2CONHO\cdot$), which leads to nitrosoformamide (NH_2CONO) [5-9]. Final products reported for the oxidation of HU are CO_2 [5-9], NH_3 [6-9] (and hydroxylamine [9]) and N_2O [6-9]. The latter would stem from the fast dimerization of unstable HNO formed during the hydrolysis of nitrosoformamide to carbamic acid (NH_2COOH) [6-9]. Chatterje et al. also detected nitrite and nitrate, which were considered as an evidence of the formation of NO during the oxidation of HU with H_2O_2.

Studies on the electrochemical oxidation of HU are rather limited. Naik et al. studied voltammetrically the process at carbon paste [10] and graphite [11] electrodes as materials for an electrochemical HU sensor. The authors assumed a two-electron oxidation leading to nitrosoformamide. Nigovic et al. studied voltammetrically the redox behavior of the iron(III)-HU complex [12]. The formation of the $NH_2CONHO\cdot$ radical upon HU oxidation was confirmed by electron paramagnetic resonance [12].

To the best of our knowledge there are no studies regarding the electrochemical behaviour of HU on metal electrodes. This contrasts with the publication of various papers dealing with the adsorption and oxidation of several related compounds such as urea [13-17], semicarbazide [18] and carbohydrazide [19]. The aim of this work is to study the electrochemistry of HU on gold electrodes in $HClO_4$ solutions. We combine voltammetric with in situ infrared experiments both under external and internal reflection conditions that can shed some light on the nature of the species formed upon

HU electrooxidation on gold. The obtained results may help in the development of an electrochemical sensor for HU based on this material.

2. Experimental Section

Solid HU (98% Calbiochem ® Merck Millipore) were dissolved in solutions made from concentrated $HClO_4$ (Merck Suprapur®) and ultrapure water (18.2 MΩ·cm, Elga Vivendi). These solutions were deaerated with Ar (N50, Air Liquide). In all the experiments, a reversible hydrogen electrode (RHE) and a gold wire were used as the reference and the counter electrode, respectively. Details of the preparation of the gold single crystals and the gold thin film electrodes are given in previous works [20,21]. Preferential (111) orientation of the evaporated gold thin films, denoted in the following as Au(111)-25 nm, has been proved in previous papers [20,22,23], and carefully checked in our experiments.

The spectroelectrochemical glass cells used in this work are equipped with a prismatic window beveled at 60° (CaF_2 or Si, for the external and internal reflection experiments, respectively) [24,25]. In situ infrared experiments were carried out using a Veemax (Pike Tech.) reflectance accessory placed in the main chamber of a Nexus 8700 (Thermo Scientific) spectrometer equipped with a MCT-A detector. Spectra were collected with a resolution of 8 cm^{-1} and are plotted in absorbance units (a.u.) as $-\log(R/R_o)$, where R and R_o represent the single beam sample and reference reflectance spectra, respectively. Positive-going and negative-going bands correspond, respectively, to gain or loss of species in the sample spectrum with respect to the reference spectrum. Sets of 100 interferograms were collected at different sample potentials and referred to a single beam spectrum collected in the HU solutions at 0.10 V.

3. Results and discussion.

Figure 1 shows cyclic voltammograms of Au(111) and Au(111)-25 nm electrodes in contact with a 10 mM HU + 0.1 M $HClO_4$ solution. After immersion of the flame-annealed Au(111) electrode at 0.10 V, the potential was cycled between 0.05 and 1.10 V, avoiding the potential range where the electrode surface is extensively oxidized. In comparison to the voltammetric response in the HU-free solution (curve a1 in Figure 1A), no significant extra contribution associated with the presence of HU is detected below 0.70 V (curve b, dashed line). However, oxidation currents appear at higher potentials, with peaks at around 0.92 and 1.00 V in the first positive-going sweep (curve c), which are related to the presence of HU. The complex shape of the voltammetric profile suggests the existence of oxidation processes involving adsorbed species as well as some degree of transport control. Moreover, the observed oxidation currents steadily decrease with cycling between 0.10 and 1.10 V. Figure 1B shows the voltammetric behavior of the Au(111)-25nm electrode in the 10 mM HU + 0.1 M $HClO_4$ solution. As expected from the preferential (111) orientation of this thin film electrode [20,22,23], the voltammograms have shapes similar to those described above for the Au(111) single crystal electrode.

Figure 2 shows sets of potential-dependent external-reflection infrared spectra collected with p- or s-polarized light for Au(111) electrode in a 10 mM HU + 0.1 M $HClO_4$ solution. The reported spectra were obtained at various potentials from 0.10 V up to 1.10 V with the flame-annealed electrode. Taking into account the time needed to collect each spectrum (around 60 s), it can be assumed that the latter are mostly related to the stationary voltammetric behavior shown in Figure 1A (curves e). The spectra at potentials below 0.70 V show features around 1600 cm^{-1}, related to changes in the baseline in the O-H bending region of water, as well as some random features in the region between 2300 and 2400 cm^{-1} associated with fluctuations during the purging of gaseous CO_2 inside the instrument. At potentials above 0.70 V, well-defined positive-going bands appear at ca. 2345 and 2231 cm^{-1} irrespective of the beam polarization. The intensities of these bands increase as the

electrode potential is raised up to 1.10 V. Taking into account the surface selection rule for external reflection infrared spectroscopy experiments on metal surfaces [26], that precludes the observation of adsorbates when using a s-polarized beam, it can be concluded that the former bands correspond to dissolved species. The feature at 2345 cm^{-1} clearly stems from the asymmetric OCO stretching of dissolved CO_2. The frequency of the feature at ca. 2230 cm^{-1} fits with that of the CN stretching mode of cyanamide ($NCNH_2$). The latter species was proposed to be a product of the electrooxidation of semicarbazide ($H_2NCONHNH_2$) [18]. A more sound assignment would relate the band at 2230 cm^{-1} either to the asymmetric NCO stretching of isocyanic acid (HNCO) [27] or to the N-N stretching of nitrous oxide (vide infra) [28].

Another feature found for the Au(111) electrode in Figure 2 is the band at ca. 2160 cm^{-1}. Despite its low intensity, this band seems to appear in the spectra collected above 0.60 V with p-polarised light. According to the surface selection rule, its absence in the s-light spectra indicates that it corresponds to a vibration of an adsorbed species. Moreover, that frequency fits with that of the band observed for gold electrodes in the presence of cyanate anions [27,29-31]. DFT calculations [27] have confirmed previous assignments of the band at ca. 2160 cm^{-1} to the asymmetric OCN stretching of N-bonded cyanate anions.

The absorption band at 2160 cm^{-1} in the spectra collected in HU-containing solutions is much more clearly appreciated in the ATR-SEIRA for a Au(111)-25nm electrode (Figure 3). The surface specificity of ATR-SEIRAS confirms that the latter feature corresponds to an adsorbed species, proving as well that the bands at 2230 and 2345 cm^{-1} in Figure 2 correspond to non-adsorbed species (the former is not observed in Figure 3 whereas the latter appears as a very small feature in the spectra collected at the more positive potentials). Some of the bands in Figure 3 are typical of the gold electrode in the $HClO_4$ solution [32], namely that for the bending mode of displaced water molecules (negative-going band around 1610 cm^{-1}) which is paralleled by the corresponding O-H stretching bands between 3000 and 3500 cm^{-1}. However, it is worth noting in Figure 3 the absence of

a band for co-adsorbed perchlorate at ca. 1100 cm^{-1}. This behavior can be connected to the strong adsorption of other species, such as adsorbed cyanate. The steadily increase of the intensity of the adsorbed cyanate band (at ca. 2160 cm^{-1}) up to 1.1 V, paralleled by a continuous blue-shift of its frequency, attaining values above 2200 cm^{-1}, are indicative of increasing cyanate coverage with electrode potential.

The spectra in Figure 3 show other positive-going bands that cannot be clearly observed in the external reflection spectra. These bands, at 1790 cm^{-1} (with a shoulder at 1810 cm^{-1}) and ca. 1405 cm^{-1}, can be related to the existence of intermediate species formed during the oxidation of HU. Another band seems to appear at ca 1675-1650 cm^{-1}, overlapping with that for the bending mode of interfacial water at ca. 1650 cm^{-1}. The existence of this contribution is confirmed by experiments in D_2O solutions (not shown).

The analysis of the spectra in figures 2 and 3 sheds some light on the HU oxidation reaction at gold electrodes. The external reflection experiments show clearly the formation of CO_2 whereas both external and internal reflection experiments prove the formation of adsorbed cyanate. This suggests the existence of parallel paths regarding the fate of the carbon atom in the hydroxyurea molecule. Formation of cyanate indicates the occurrence of a process that could be considered as the opposite of the hydroxyurea synthesis from hydroxylamine and cyanate [1]

$$H_2NCONHOH \rightarrow OCN^-(ads) + NH_2OH + H^+ \qquad (1)$$

This process could be driven by the potential-dependent cyanate adsorption at gold electrodes [27]. In acidic media adsorbed cyanate can be readily protonated (pK_a=3.7 [33,34]) yielding isocyanic acid in solution that explains the band at 2231 cm^{-1} in the external reflection spectra.

$$^-OCN(ads) + H^+(aq) \leftrightarrow OCNH(aq) \qquad (2)$$

Note that this band corresponds to a dissolved species, as DFT calculations have shown that isocyanic acid interacts very weakly with gold surfaces [27]. Regarding hydroxylamine, recent results by Scherson's group show that this species readily oxidizes above 0.50 V SCE on gold electrodes in $HClO_4$ solutions [35]. In situ infrared by the same group proved the formation of N_2O as witnessed by a band at 2230 cm^{-1} [28], similar to that in Figure 2. According to this result, the authors proposed a complex mechanism in neutral solutions involving the formation of N_2O either through the direct oxidation of hydroxylamine

$$2\ NH_2OH \rightarrow N_2O + H_2O + 4H^+ + 4e \qquad (3)$$

or through a chemical reaction between hydroxylamine and nitrite anions formed upon oxidation of hydroxylamine in a parallel path via nitric oxide generation.

Regarding the formation of CO_2, this could come both from the direct oxidation of HU

$$H_2NCONHOH + 2\ H_2O \rightarrow CO_2 + 2\ NH_2OH + 2\ H^+ + 2\ e \qquad (4)$$

or from that of adsorbed cyanate as proposed by Kitamura et al [36] and Yépez and Scharifker [37] at platinum electrodes according to:

$$2\ OCN^-(ads) + 2\ H_2O \rightarrow 2\ CO_2 + N_2 + 4H^+ + 6\ e \qquad (5)$$

Finally, the bands below 1850 cm^{-1} in the ATR-SEIRA spectra provide evidences for the formation of oxidation intermediates other that adsorbed cyanate. The assignment of these bands requires the calculation of geometries and frequencies for the plausible adsorbed species that could be formed upon HU reactive adsorption. From DFT results to be reported in a future paper, the well-marked band at ca. 1810 cm^{-1} can be tentatively ascribed to the N=O stretching band of adsorbed nitrosoformamide, one of the reaction intermediates for HU oxidation proposed in the literature

$$H_2NCONHOH \rightarrow H_2NCONO(ads) + 2\ H^+ + 2\ e \qquad (6)$$

4. Conclusions.

In situ infrared experiments with gold electrodes having (111) orientation evidence the formation of adsorbed cyanate anions as a product of HU electrooxidation in acidic solutions. The band at 2231 cm^{-1} in the external reflection spectra can be ascribed both to dissolved isocyanic acid formed upon protonation of cyanate anions and to N_2O generated upon further electrooxidation of the hydroxylamine formed during a chemical decomposition of HU. Dissolved CO_2 is also detected as an oxidation product in agreement with results reported for the chemical oxidation of HU. This latter species could be formed both upon the direct electroxidation of HU or as a product of the oxidation of adsorbed cyanate. The ATR-SEIRA bands appearing in the region for HU electrooxidation indicate the presence of other adsorbed intermediates. The results of DFT calculations carried out to provide support for the assignment for the observed adsorbate bands will be described in detail elsewhere.

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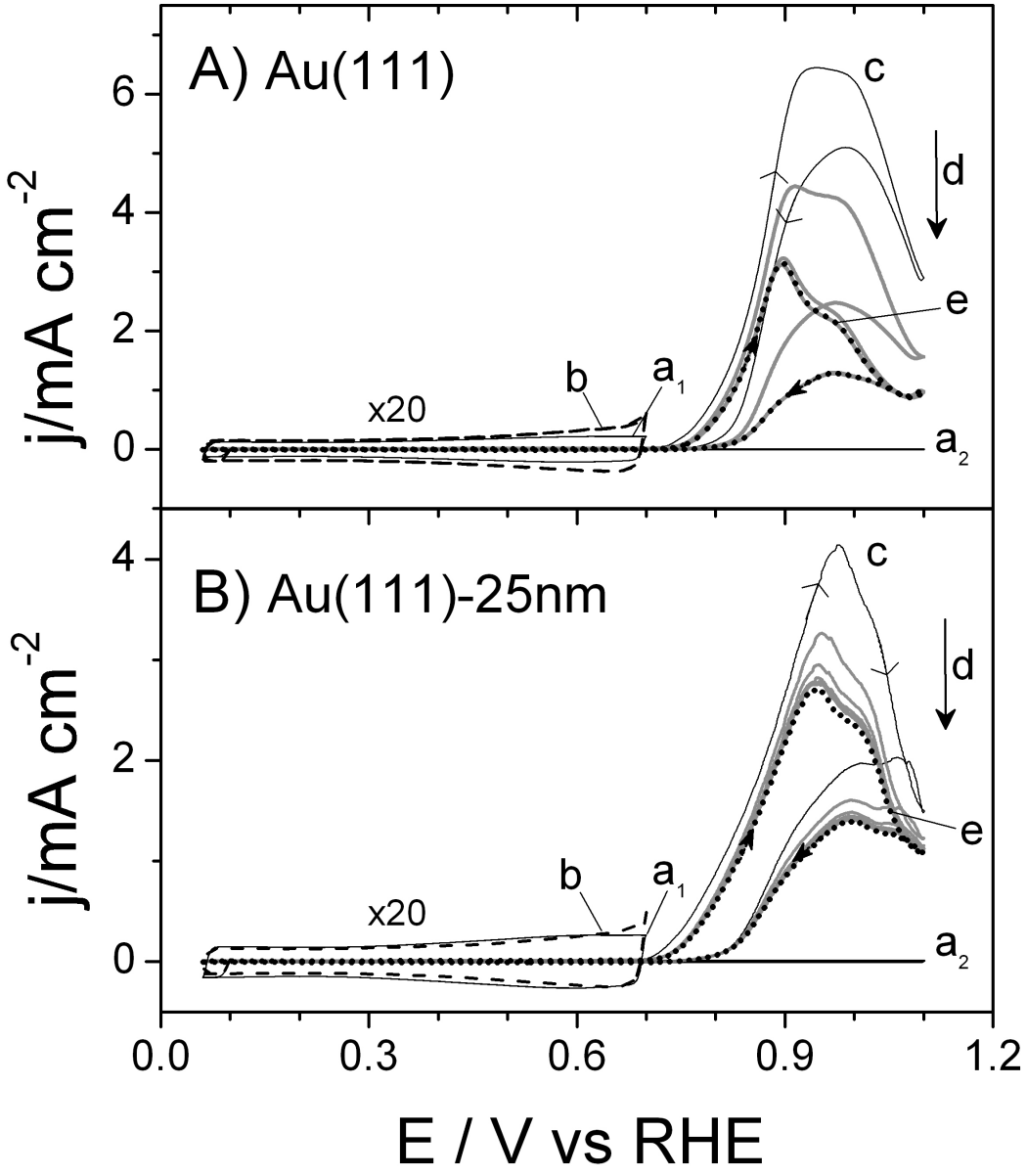

Figure 1. Cyclic voltammograms obtained for A) Au(111) and B) Au(111)-25nm electrodes in x mM HU + 0.1 M $HClO_4$ solutions with x=0 (curves a1 and a2) and 10 mM (curves b to e). Curves c and e correspond, respectively, to the first and the stationary voltammogram recorded up to 1.10 V. Curves d correspond to the second and subsequent cycles between 0.05 and 1.10 V. Immersion potentials: 0.10 V. Scan rate: 50 $mV \cdot s^{-1}$.

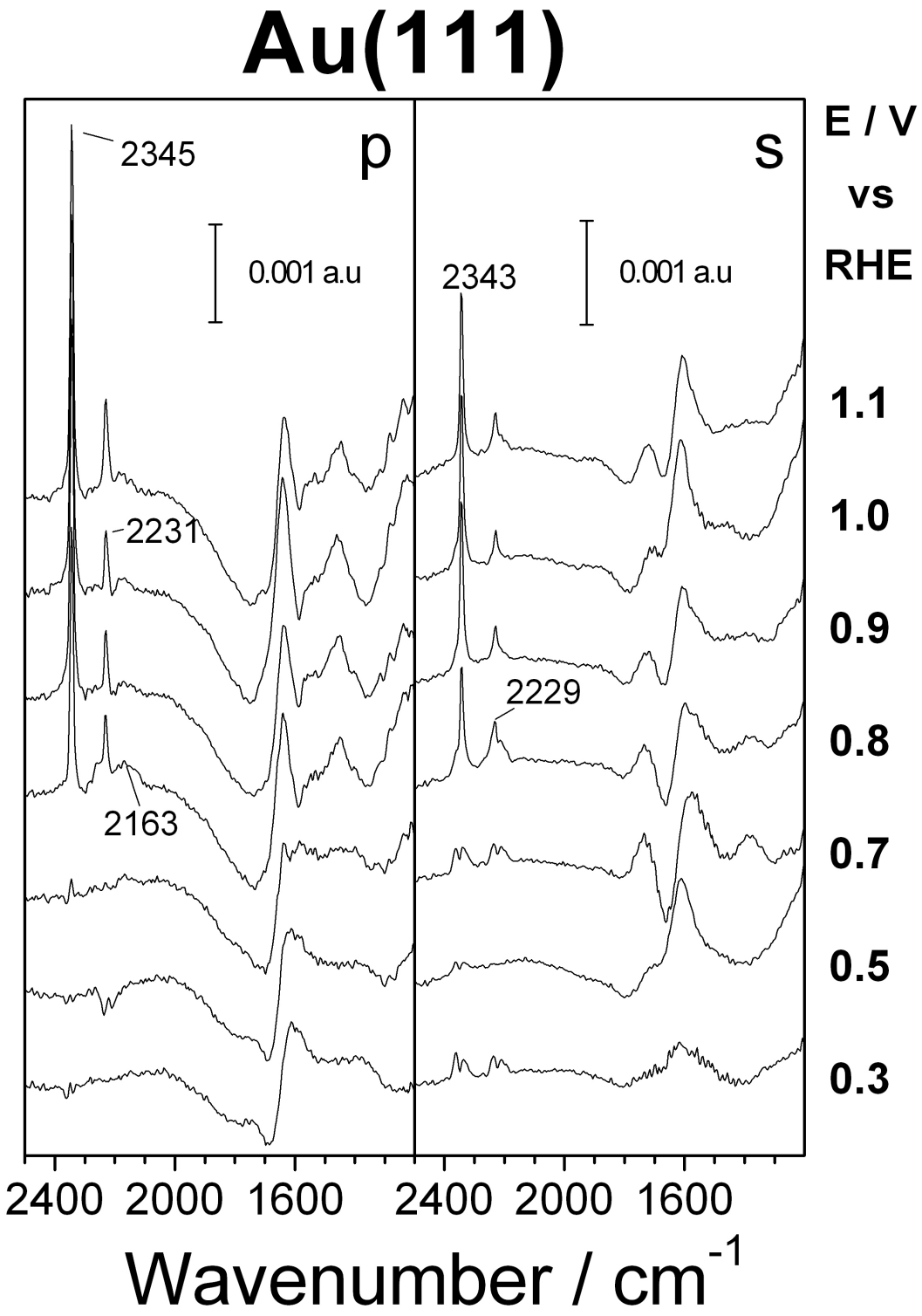

Figure 2. Potential-dependent infrared external reflection spectra collected with p- or s-polarized light for a Au(111) electrode in a 10 mM HU + 0.1 M $HClO_4$ solution.

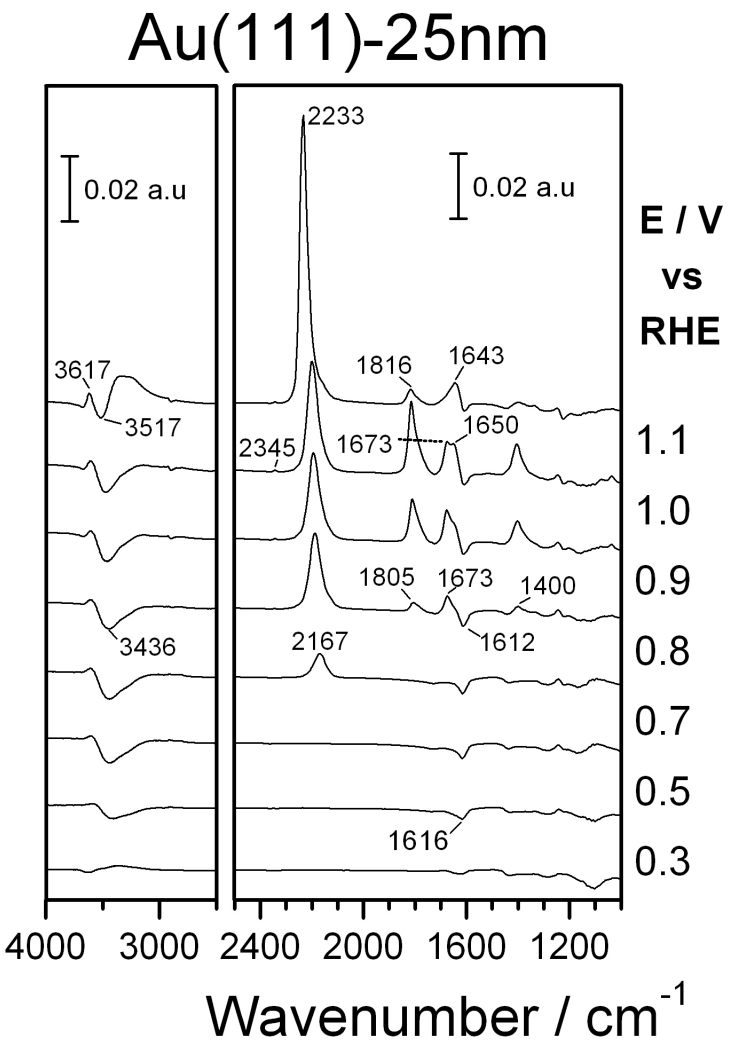

Figure 3. Potential-dependent ATR-SEIRA spectra collected with p-polarized light for a Au(111)-25nm electrode in a 10 mM HU + 0.1 M $HClO_4$ solution prepared in water.

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